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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,066	01/29/2002	Alejandro Abuin	LEX-0304-USA	8417

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EXAMINER	
BERTOGLIO, VALARIE E	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/060,066	ABUIN ET AL.	
	Examiner	Art Unit	
	Valarie Bertoglio	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *29 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment filed 07/29/2003 had been entered. Claims 3 and 7 have been amended. Claim 8 has been cancelled. Claims 1-7 are pending and under examination in the instant office action.

Claim Rejections - 35 USC § 101/ 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility.

This rejection is maintained for reasons of record as stated on pages 2-5 of the prior office action mailed 02/25/2003.

Applicant's arguments are not persuasive. Applicant argues that "The practical implementation of the present invention adds value to human genomic data by assigning critical functional annotation to the human sequence data" (refer to Amendment received 07/29/2003, page 4, lines 5-6). While those of ordinary skill in the art may be using applicant's **technique** or **methodology** to study genes, they are not using applicant's particularly claimed cell lines having the particularly claimed sequences mutated. This particular cell line has no well-known use in the absence of further characterization of the cell line itself. The instant application appears to be an invitation for trial and error experimentation to determine the specific function of the protein product encoded by the claimed nucleotide sequences, and from there to determine uses based on that function. In Brenner, the Court held that materials to be used as an object of

research or methods of using those materials as an object for research have raised issues as to whether those materials possess a real world context of use of substantial utility. See Brenner v. Manson, 148 USPQ 689 (US SupCt 1966).

The whole of the specification is directed to taking the cell line generated by the gene trapping technique and **determining what the identity and function** of the particular gene trapped is so as to **potentially** provide useful information for therapeutic or diagnostic applications. The evidence of record at the time the claimed invention was filed, had not disclosed the identity or function of a gene comprising SEQ ID NO:2. Applicant argues that SEQ ID NO:2 encodes the murine ortholog of a human gene encoding the human calcium channel, voltage-dependent, gamma subunit 8 (CACNG8) gene. The evidence of record at the time the invention was made does not disclose the identity or function of the gene. The specification, as filed, fails to support that SEQ ID NO:2 encodes the murine ortholog of CACNG8. The MPEP states that the arguments of counsel cannot take the place of evidence in the record . In re Schulze, 346 F.2d 600, 602, 145 USPQ 716,718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results. MPEP 716.01(c).

Applicants argue further that the claimed cell line was used to produce homozygous mutant animals, and as a result of the disruption, the animal displayed hyperactivity. Thus, applicants argue that the claimed ES cells can be used to generate an animal that is useful for identifying pharmaceuticals (refer to Amendment received 06/05/2003, page 4, lines 17-24).

In response to applicant's arguments, the mouse derived from ES cells comprising an engineered mutation in a gene corresponding to SEQ ID NO:2, as recited in the amendment

received 07/29/2003, page 4, lines 14-18, is not described in the specification of the instant invention. Without having the described animal derived from ES cells comprising an engineered mutation in a gene corresponding to SEQ ID NO:2 on the record, it cannot be assumed or predicted that the animals display a phenotype of hyperactivity or any other phenotype and thus, applicants' arguments do not support a use for the claimed ES cells. Further experimentation is required to determine what the direct or indirect effects of mutating the gene corresponding to SEQ ID NO: 2 will be. Thus, the evidence of record fails to support the asserted utility of the claimed ES cells. Applicants have failed to point to a specific or substantial utility for the claimed invention and have failed to provide evidence of the phenotype asserted on page 4, lines 17-24 of the Amendment received 06/05/2003. The claimed invention does not have a substantial utility because the specification does not show how to use the claimed cells without resorting to additional research to determine the function of the gene whose expression is reduced in the claimed cell, nor is it predictable if the function of the gene were determined, that a cell with reduced expression of the gene would have a practical use. Again, the MPEP states that the arguments of counsel cannot take the place of evidence in the record . In re Schulze, 346 F.2d 600, 602, 145 USPQ 716,718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results. MPEP 716.01(c).

Applicants also argue that the technique of gene targeting was awarded the Lasker Award, highlighting the well established and credible utility of the claimed mutated ES cell line. Applicants argue further that the U.S. government has "validated" the usefulness of the technique of gene trapping by providing millions of dollars to the technique. These arguments

are not persuasive and are not relevant to the rejection. While the techniques of gene trapping and generating mutations in ES cells are necessary in revealing important genes for further research, the cell lines harboring mutations in uncharacterized genes have no patentable utility without knowing the identity and function of the gene in question.

It is maintained that the claimed mouse ES cell lines lack a specific and substantial utility until the gene is further characterized and identified as to its function. No genotype or phenotype of record is associated with SEQ ID NO:2. No gene function (or disruption thereof) is disclosed for any gene comprising the nucleotide sequence set forth in SEQ ID NO:2. The claimed product cannot be considered a research tool but rather is a material to be experimented upon.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial, and credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. In light of the amendments to the claims filed 06/05/2003, the rejection based on the failure to adequately describe the broad genera of species encompassed by the claims has been withdrawn.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

invention. Claim 1 encompasses a gene "identifiable as corresponding to SEQ ID NO:2". As it is not apparent that SEQ ID NO: 2 is a complete cDNA sequence, the claims read on all cells that have a disruption of any gene comprising an undescribed sequence. A gene "identifiable as corresponding to SEQ ID NO:2" encompasses a large genera of sequences of which each of the encompassed sequences merely comprises SEQ ID NO:2 in addition to other undescribed sequences that make up the claimed gene. For example, the specification does not describe promoter sequences, intron/exon boundaries or 5' and 3' UTR for the claimed genera. Many, if not most, of the sequences encompassed may not be real sequences corresponding to real genes. The claims require that one of ordinary skill in the art produce murine ES cell lines, which comprise a disruption of a gene whose sequence may not exist in nature. The skilled artisan cannot envision the detailed chemical structures of all the sequences encompassed by the above noted SEQ ID NO: 2.

Applicants argue that the sequence reported in SEQ ID NO: 2 represents exon sequence that clearly identifies the gene that has been mutated in the described ES cell line (page 10, lines 12-15). This argument is not persuasive as it fails to address the rejection set forth above. The genes comprising an exon sequence disclosed in SEQ ID NO: 2 encompassed by the genus have not been disclosed. It is not apparent that the sequence set forth in SEQ ID NO: 2 is a complete gene sequence and therefore the claim is directed to a large genera of genes wherein the complete nucleotide sequence of the gene, including nucleotide sequence outside of that set forth by SEQ ID NO:2 is not known. There is no evidence of record of a relationship between the structure of any gene and the sequence set forth in SEQ ID NO: 2 that would provide any reliable information about the structure of any gene within the genus. There is no evidence on the record

that the nucleotide sequence set forth by SEQ ID NO: 2 had a known structural relationship to any gene sequence. In view of the above considerations, one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by a member of the genus because partial coding sequence as set forth by SEQ ID NO: 2 is not representative of any gene within the claimed genus.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Valarie Bertoglio whose telephone number is 703-305-5469. The examiner can normally be reached on Mon-Weds 6:00-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on 703-305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Valarie Bertoglio
Examiner
Art Unit 1632

Deborah Reynolds
DEBORAH J. REYNOLDS
SUPERVISORY PATENT EXAMINER
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